Polycystic Kidney Disease

National Kidney and Urologic Diseases Information Clearinghouse

National Institute of Diabetes and Digestive and Kidney Diseases

NATIONAL INSTITUTES OF HEALTH

Polycystic kidney disease (PKD) is a genetic disorder characterized by the growth of numerous cysts in the kidneys. The cysts are filled with fluid. PKD cysts can slowly replace much of the mass of the kidneys, reducing kidney function and leading to kidney failure.

The kidneys are two organs, each about the size of a fist, located in the upper part of a person's abdomen, toward the back. The kidneys filter wastes and extra fluid from the blood to form urine. They also regulate amounts of certain vital substances in the body.

When PKD causes kidneys to fail—which usually happens after many years—the patient requires dialysis or kidney transplantation. About one-half of people with the major type of PKD progress to kidney failure, also called end-stage renal disease (ESRD).

PKD can cause cysts in the liver and problems in other organs, such as the heart and blood vessels in the brain. These complications help doctors distinguish PKD from the usually harmless "simple" cysts that often form in the kidneys in later years of life.

In the United States, about 600,000[1] people have PKD, and it is the fourth leading cause of kidney failure. Medical professionals describe two major inherited forms of PKD and a noninherited form:

- **Autosomal dominant PKD** is the most common inherited form. Symptoms usually develop between the ages of 30 and 40, but they can begin earlier, even in childhood. About 90 percent of all PKD cases are autosomal dominant PKD.
- **Autosomal recessive PKD** is a rare inherited form. Symptoms of autosomal recessive PKD begin in the earliest months of life, even in the womb.
- **Acquired cystic kidney disease (ACKD)** develops in association with long-term kidney problems, especially in patients who have kidney failure and who have been on dialysis for a long time. Therefore it tends to occur in later years of life. It is not an inherited form of PKD.

Autosomal Dominant PKD

What is autosomal dominant PKD?

Autosomal dominant PKD is one of the most common inherited disorders. The phrase "autosomal dominant" means that if one parent has the disease, there is a 50-percent chance that the disease will pass to a child (see *Genetic Diseases*). In some rare cases, the cause of autosomal dominant PKD occurs spontaneously in the child soon after conception—in these cases, the parents are not the source of the disease.

Many people with autosomal dominant PKD live for decades without developing symptoms. For this reason, autosomal dominant PKD is often called "adult polycystic kidney disease." Yet, in some cases, cysts may form earlier, even in the first years of life.

[1] Grantham JJ, Nair V, Winklhoffer F. Cystic diseases of the kidney. In: Brenner BM, ed. *Brenner & Rector's The Kidney.* Vol. 2. 6th ed. Philadelphia: W.B. Saunders Company; 2000: 1699–1730.

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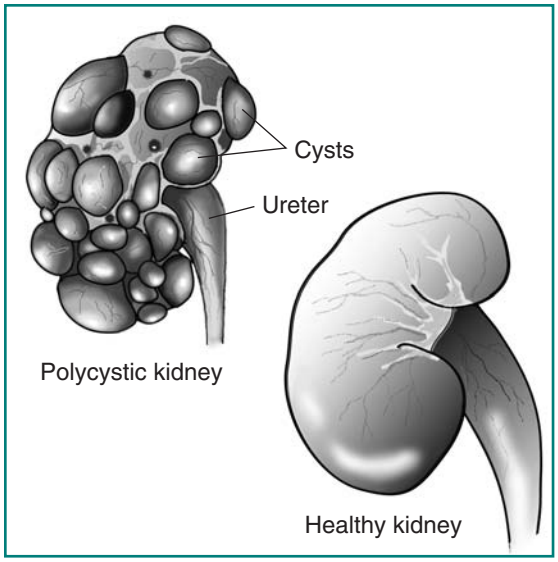


The polycystic kidney roughly retains the same shape as the healthy kidney.

The cysts grow out of nephrons, the tiny filtering units inside the kidneys. The cysts eventually separate from the nephrons and continue to enlarge. The kidneys enlarge along with the cysts—which can number in the thousands—while roughly retaining their kidney shape. In fully developed PKD, a cyst-filled kidney can weigh as much as 22 pounds. High blood pressure occurs early in the disease, often before cysts appear.

What are the symptoms of autosomal dominant PKD?

The most common symptoms are pain in the back and the sides—between the ribs and hips—and headaches. The pain can be temporary or persistent, mild or severe.

People with autosomal dominant PKD also can experience the following complications:

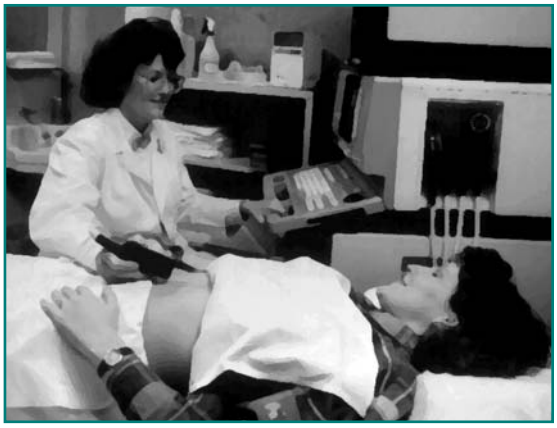
- urinary tract infections
- hematuria—blood in the urine
- liver and pancreatic cysts
- abnormal heart valves
- high blood pressure
- kidney stones
- aneurysms—bulges in the walls of blood vessels—in the brain
- diverticulosis—small sacs on the colon

How is autosomal dominant PKD diagnosed?

To diagnose autosomal dominant PKD, a doctor typically observes three or more kidney cysts using ultrasound imaging. The diagnosis is strengthened by a family history of autosomal dominant PKD and the presence of cysts in other organs.

In most cases of autosomal dominant PKD, the physical condition appears normal for many years, even decades, so the disease can go unnoticed. Physical checkups and blood and urine tests may not lead to diagnosis. The slow, undetected progression is why some people live for many years without knowing they have autosomal dominant PKD.

Once cysts have formed, however, diagnosis is possible with imaging technology. Ultrasound, which passes sound waves through the body to create a picture of the kidneys, is used most often. Ultrasound imaging does not use any injected dyes or radiation and is



An ultrasound imaging device passes harmless sound waves through the body to detect possible kidney cysts.

safe for all patients, including pregnant women. It can also detect cysts in the kidneys of a fetus.

More powerful and expensive imaging procedures such as computerized tomography (CT) scans and magnetic resonance imaging (MRI) also can detect cysts. Recently, MRI has been used to measure kidney and cyst volume and monitor kidney and cyst growth.

A genetic test can detect mutations in the *PKD1* and *PKD2* genes. Although this test can detect the presence of the autosomal dominant PKD mutations before cysts develop, its usefulness is limited by two factors: It cannot predict the onset or ultimate severity of the disease, and no absolute cure is available to prevent the onset of the disease. However, a young person who knows of a PKD gene mutation may be able to forestall the disease through diet and blood pressure control. The test may also be used to determine whether a young member of a PKD family can safely donate a kidney to a parent. Anyone considering genetic testing should receive counseling to understand all the implications of the test.

How is autosomal dominant PKD treated?

Although a cure for autosomal dominant PKD is not available, treatment can ease the symptoms and prolong life.

Pain. A doctor will first suggest over-the-counter pain medications, such as aspirin or acetaminophen (Tylenol). Consult your doctor before taking any over-the-counter medication because some may be harmful to the kidneys. For most but not all cases of severe pain, surgery to shrink cysts can relieve pain in the back and flanks. However, surgery provides only temporary relief and usually does not slow the disease's progression toward kidney failure.

Headaches that are severe or that seem to feel different from other headaches might be caused by aneurysms—blood vessels that balloon out in spots—in the brain. Headaches also can be caused by high blood pressure. People with autosomal dominant PKD should see a doctor if they have severe or recurring headaches—even before considering over-the-counter pain medications.

Urinary tract infections. People with autosomal dominant PKD tend to have frequent urinary tract infections, which can be treated with antibiotics. People with the disease should seek treatment for urinary tract infections immediately because infection can spread from the urinary tract to the cysts in the kidneys. Cyst infections are difficult to treat because many antibiotics do not penetrate into the cysts.

High blood pressure. Keeping blood pressure under control can slow the effects of autosomal dominant PKD. Lifestyle changes and various medications can lower high blood pressure. Patients should ask their doctors about such treatments. Sometimes proper diet and exercise are enough to keep blood pressure controlled.

End-stage renal disease. After many years, PKD can cause the kidneys to fail. Because kidneys are essential for life, people with ESRD must seek one of two options for replacing kidney functions: dialysis or transplantation. In hemodialysis, blood is circulated into an external filter, where it is cleaned before reentering the body; in peritoneal dialysis, a fluid is introduced into the abdomen, where it absorbs wastes and is then removed. Transplantation of healthy kidneys into ESRD patients has become a common and successful procedure. Healthy kidneys transplanted into PKD patients do not develop cysts.

Autosomal Recessive PKD

What is autosomal recessive PKD?

Autosomal recessive PKD is caused by a particular genetic trait that is different from the genetic trait that causes autosomal dominant PKD. Parents who do not have PKD can have a child with the disease if both parents carry the abnormal gene and both pass the gene to their baby. The chance of the child having autosomal recessive PKD when both parents carry the abnormal gene is 25 percent. If only one parent carries the abnormal gene, the baby cannot get autosomal recessive PKD.

The signs of autosomal recessive PKD can begin before birth, so it is often called "infantile PKD." Children born with autosomal recessive PKD usually develop kidney failure within a few years. Severity of the disease varies. Babies with the worst cases die hours or days after birth. Children with an infantile version may have sufficient renal function for a few years. Some people with autosomal recessive PKD do not develop symptoms until later in childhood and may live into their teens and twenties. People with this juvenile version also usually have liver problems.

What are the symptoms of autosomal recessive PKD?

Children with autosomal recessive PKD experience high blood pressure, urinary tract infections, and frequent urination. The disease usually affects the liver, spleen, and pancreas, resulting in low blood cell counts, varicose veins, and hemorrhoids. Because kidney function is crucial for early physical development, children with autosomal recessive PKD are usually smaller than average size.

How is autosomal recessive PKD diagnosed?

Ultrasound imaging of the fetus or newborn reveals cysts in the kidneys but does not distinguish between the cysts of autosomal recessive and autosomal dominant PKD. Ultrasound examination of kidneys of relatives can be helpful; for example, a parent or grandparent with autosomal dominant PKD cysts could help confirm diagnosis of autosomal dominant PKD in a fetus or child. It is extremely rare, although not impossible, for a person with autosomal recessive PKD to live long enough to become a parent. Because autosomal recessive PKD tends to scar the liver, ultrasound imaging of the liver also aids in diagnosis.

Genetic Diseases

Genes are segments of DNA, the long molecules that reside in each of your body's cells. The genes, through complex processes, build proteins for growth and maintenance of the body. At conception, DNA—or genes—from both parents are passed to the child.

A genetic disease occurs when one or both parents pass abnormal genes to a child at conception. If receiving an abnormal gene from just one parent is enough to produce a disease in the child, the disease is said to have dominant inheritance. If receiving abnormal genes from both parents is needed to produce disease in the child, the disease is said to be recessive.

The chance of acquiring a dominant disease is higher than the chance of acquiring a recessive disease. A child who receives only one gene copy for a recessive disease at conception will not develop the genetic disease—such as autosomal recessive PKD—but could pass the gene to the following generation.

How is autosomal recessive PKD treated?

Medicines can control high blood pressure in autosomal recessive PKD, and antibiotics can control urinary tract infections. Eating increased amounts of nutritious food improves growth in children with autosomal recessive PKD. In some cases, growth hormones are used. In response to kidney failure, autosomal recessive PKD patients must receive dialysis or transplantation.

Acquired Cystic Kidney Disease

What is ACKD?

ACKD develops in kidneys with long-term damage and severe scarring, so it often is associated with dialysis and ESRD. About 90 percent of people on dialysis for 5 years develop ACKD. People with ACKD can have any underlying kidney disease, such as glomerulonephritis or kidney disease of diabetes. The cysts of ACKD may bleed.

People with ACKD are twice as likely as people in the general population to develop kidney cancer. Even with this increased risk, however, kidney cancer is rare.

How is ACKD diagnosed?

People with ACKD usually seek help because they notice blood in their urine, a condition called hematuria. The cysts bleed into the urinary system, which discolors urine. Diagnosis is confirmed using ultrasound, CT scan, or MRI of the kidneys.

How is ACKD treated?

Most people with ACKD are already receiving treatment for kidney problems. In rare cases, surgery is used to stop bleeding of cysts and to remove tumors or suspected tumors.

Hope Through Research

Scientists have begun to identify the processes that trigger formation of PKD cysts. Advances in the field of genetics have increased our understanding of the abnormal genes responsible for autosomal dominant and autosomal recessive PKD. Scientists have located two genes associated with autosomal dominant PKD. The first was located in 1985 on chromosome 16 and labeled *PKD1*. *PKD2* was localized to chromosome 4 in 1993. Within 3 years, scientists had isolated the proteins these two genes produce—polycystin-1 and polycystin-2.

When both the *PKD1* and *PKD2* genes are normal, the proteins they produce work together to foster normal kidney development and inhibit cyst formation. A mutation in either of the genes can lead to cyst formation, but evidence suggests that the disease development also requires other factors, in addition to the mutation in one of the PKD genes.

Genetic analyses of most families with PKD confirm mutations in either the *PKD1* or *PKD2* gene. In rare cases, however, families with PKD have been found to have normal *PKD1* and *PKD2* genes. As a result, researchers theorize that a *PKD3* gene exists, but that gene has not been mapped or identified.

Researchers recently identified the autosomal recessive PKD gene, called *PKHD1,* on chromosome 6. No genetic test is available to detect mutations in *PKHD1.*

Researchers have bred mice with a genetic disease that parallels both inherited forms of human PKD. Studying these mice will lead to greater understanding of the genetic and nongenetic mechanisms involved in cyst formation. In recent years, researchers have discovered two separate compounds that appear to inhibit cyst formation in mice with

the PKD gene. Scientists hope further testing will lead to safe and effective treatments for humans.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is supporting the Consortium for Radiologic Imaging Studies of PKD (CRISP), a team of scientists from universities across the country. The CRISP project uses advanced medical imaging techniques to measure the rate of cyst and kidney growth in PKD. The CRISP scientists have already determined that kidney growth in people with PKD is continuous. In other words, kidney growth happens gradually and steadily from childhood to adulthood, not in spurts. Also, the rate of kidney growth corresponds to the rate of decline in kidney function for people with PKD. This knowledge will be useful in monitoring the effectiveness of experimental treatments as they are tested.

The NIDDK and the PKD Foundation are supporting HALT PKD, a clinical trial to determine whether the use of two blood pressure medicines—an angiotensin-converting enzyme (ACE) inhibitor and an angiotensin receptor blocker (ARB)—is more effective at slowing the progression of PKD than standard antihypertensive therapy. The trial will also determine whether a low blood pressure target (95–110/60–75 mm Hg) protects the kidneys longer than a standard blood pressure target (120–130/70–80 mm Hg) in people with PKD.

People interested in participating in clinical trials of new treatments for PKD can find a list of centers recruiting patients at *www.ClinicalTrials.gov.*

Points to Remember

The three types of polycystic kidney disease (PKD) are

- two inherited forms:
  - autosomal dominant PKD, a common form that usually causes symptoms in midlife
  - autosomal recessive PKD, a rare form that usually causes symptoms in early childhood
- acquired cystic kidney disease, a noninherited form associated with long-term kidney problems, dialysis, and old age

The symptoms and signs of PKD include

- pain in the back and lower sides
- headaches
- urinary tract infections
- blood in the urine
- cysts in the kidneys and other organs

Diagnosis of PKD is obtained by

- ultrasound imaging of kidney cysts
- ultrasound imaging of cysts in other organs
- family medical history, including genetic testing

PKD has no cure. Treatments include

- medicine and surgery to reduce pain
- antibiotics to resolve infections
- dialysis to replace functions of failed kidneys
- kidney transplantation

For More Information

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Email: pkdcure@pkdcure.org
Internet: www.pkdcure.org

American Association of Kidney Patients
3505 East Frontage Road, Suite 315
Tampa, FL 33607
Phone: 1–800–749–2257 or 813–636–8100
Email: info@aakp.org
Internet: www.aakp.org

National Kidney Foundation, Inc.
30 East 33rd Street
New York, NY 10016
Phone: 1–800–622–9010 or 212–889–2210
Internet: www.kidney.org

You may also find additional information on this topic using the following databases:

The NIDDK Reference Collection is a collection of thousands of materials produced for patients and health care professionals, including fact sheets, brochures, and audiovisual materials. Visit *www.catalog.niddk.nih.gov/resources.*

MedlinePlus brings together a wealth of information from the National Library of Medicine, the National Institutes of Health, and other government agencies and health-related organizations. MedlinePlus offers easy access to medical journal articles, a medical dictionary and medical encyclopedia, health information in Spanish, hospital and physician directories, drug and supplement lists, interactive patient tutorials, links to hundreds of clinical trials, and the latest health news. Visit *www.medlineplus.gov.*

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Publications produced by the Clearinghouse are carefully reviewed by both NIDDK scientists and outside experts.

This fact sheet is also available at *www.kidney.niddk.nih.gov.*

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

NIH Publication No. 07–4008
June 2007